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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/584,425	05/30/2007	Tomoko Ono	2352.014	1952

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HESLIN ROTHENBERG FARLEY & MESITI PC
5 COLUMBIA CIRCLE
ALBANY, NY 12203

EXAMINER	
GABEL, GAILENE	

ART UNIT	PAPER NUMBER
1641	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/584,425	ONO ET AL.	
	Examiner	Art Unit	
	GAILENE R. GABEL	1641	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *12 March 2010*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,3 and 5-10* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1 and 5-9* is/are rejected.

7)☒ Claim(s) *3 and 10* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *22 June 2006 and 12 March 2010* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Amendment Entry

1. Applicant's amendment and response filed March 12, 2010, is acknowledged and has been entered. Claims 1 and 6 have been amended. Claims 2 and 4 have been cancelled. Claims 7-10 have been added. Accordingly, claims 1, 3 and 5-10 are pending and are under examination.

Claim Rejections / Objections

2. All rejections or objections not reiterated herein have been withdrawn.

3. The rejections of claims 2 and 4 are now moot in light of Applicant's cancellation of the claims.

4. The rejection of claims 1, 3, 5 and 6 under 35 U.S.C. 102(e) as being anticipated by Igami et al. (US 2009/0220990) is now moot in light of Applicant's submission of a Certified Translation of the Priority Document JP 2003-425706.

5. In light of Applicant's argument, the rejection of claims 1, 5, and 6 under 35 U.S.C. 102(a) as being anticipated by Soejima et al. (EP 1 544 293), is hereby, withdrawn.

New Grounds of Rejection

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

6. Claims 1, 3, 5, and 7-10 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 1 is objected to in reciting, " promyelotic." It should recite, "promyelocytic."

Claim 1 is confusing because the method concludes with "correlating ... with a lower level [of von Willebrand factor- cleaving protease] in the sample being indicative of an increased risk of thrombophilia" whereas the preamble recites, "A method of detecting and analyzing the degree of thrombophilia." Therefore, it is unclear as to whether the claimed method intends a method of detecting and analyzing the degree of thrombophilia or a method of indicating increased risk of thrombophilia in a patient.

Claim 1 is ambiguous in reciting, "patient suffering from one or more of the following conditions acute or chronic myeloid leukemia, acute promyelocytic leukemia, pulmonary, embolism, cerebral infarction, veno-occlusive disease, acute lymphocytic leukemia, and deep vein thrombosis" because it is unclear how these listed diseases are "conditions" and how these listed diseases should structurally and functionally relate to vWF-cp and to either one of "degree of thrombophilia" or "increased risk of thrombophilia" as claimed.

Claim 7 is confusing because the method concludes with "correlating ... with a lower level [of von Willebrand factor- cleaving protease] in the sample being indicative of an increased risk of thrombophilia" whereas the preamble recites, "A method of analyzing a degree of thrombophilia." Therefore, it is unclear as to whether the claimed

method intends a method of analyzing degree of thrombophilia or a method of indicating increased risk of thrombophilia in a patient.

Claim 8 recites improper Markush language in reciting, "where the bodily fluid is selected from a group comprising ... or ...." Perhaps, Applicant intends "where the bodily fluid is selected from the group consisting of ... and ..." for proper Markush language.

Claim 9 is objected to in reciting, " promyelotic." It should recite, "promyelocytic."

Claim 9 is ambiguous in relation to claim 7 in reciting, "the patient is a person suffering from one or more of the following ... "conditions" acute or chronic myeloid leukemia, acute promyelocytic leukemia, pulmonary, embolism, cerebral infarction, veno-occlusive disease, acute lymphocytic leukemia, and deep vein thrombosis" because it is unclear how these listed diseases are "conditions" and how these listed diseases should structurally and functionally relate to vWF-cp and to either one of "degree of thrombophilia" or "increased risk of thrombophilia" as recited in claim 7 from which it depends.

Scope of Enablement

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

7. Claims 7-10 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabled for blood plasma as bodily fluid, does not reasonably

provide enablement for any other body fluid such as cell or tissue fluids, lymph, a thymic fluid, ascites fluid, an amniotic fluid, gastric juices, urine, pancreatic juices, spinal fluid, and saliva. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims.

As set forth in In re Wands, 858 F .2d 731, 8 USPQ2d 1400 (Fed. Cir. 1988), enablement requires that the specification teach those in the art to make and use the invention without undue experimentation. Factors to be considered in determining whether a disclosure would require undue experimentation include 1) the nature of the invention, 2) the state of the prior art, 3) the predictability or lack thereof in the art, 4) the amount of direction or guidance present, 5) the presence or absence of working examples, 6) the quantity of experimentation necessary, 7) the relative skill of those in the art, and 8) the breadth of the claims.

As to bodily fluids for use in the method, the direction and guidance in the specification is notably limited to measuring von Willebrand factor-cleaving protease (vWF-cp) in blood plasma samples. The working examples are also limited to use of plasma samples to determine the level of vWF-cp for comparison with levels obtained from blood plasma of healthy control subjects. Although paragraph [0042] of Applicant's disclosure lists use of other fluids such as cell or tissue fluids, lymph, a thymic fluid, ascites fluid, an amniotic fluid, gastric juices, urine, pancreatic juices, spinal fluid, and saliva, nowhere in the specification provides normal control levels of vWF-cp in these sample sources from healthy control subjects. Additionally, nowhere in the specification

shows the claimed decreased results of vWF-cp obtained from patient samples. Paragraph [0065] shows using blood plasma samples only from dialysis patients to measure vWF-cp for comparison with that of healthy control subjects. Based on this limited disclosure and direction, one of skill in the art would not know how to use alternative bodily fluid samples such as urine as claimed, without undue experimentation.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.

8. Claims 1 and 5-9 are rejected under 35 U.S.C. 102(a) as being anticipated by Scheiflinger et al. (US 2004/0214346 A1).

Scheiflinger et al. disclose a kit and diagnostic method for detecting and determining diagnosis of thrombosis manifested in a patient blood plasma sample by measuring the amount of von Willebrand factor-cleaving protease (vWF-cp) in the plasma sample [0015, 0029, 0032]. Thrombosis may be manifested in patients suffering from thrombotic microangiopathy (TM) and other cancer-associated TM (i.e. acute or chronic myeloid leukemia, acute lymphocytic leukemia) [0034]. In practice, Scheiflinger et al. teach combining a blood sample from the patient with anti-vWFcp antibody that specifically binds to vWFcp immobilized into a solid phase and then

detecting binding and complex formation of the anti-vWFcp antibody to vWFcp antigen using the immunological assay kit and method. The amount of vWFcp that bound to the anti-vWF antibody is also measured [0032]. Scheiflinger et al. show that a decrease in concentration of vWFcp in a patient in comparison to healthy control provides indication of occurrence of thrombosis ([0055, 0056]; Table 3).

As to the recitation of "degree of thrombophilia" or "risk of thrombophilia," it is well understood that "thrombophilia" or hypercoagulability is simply a measure of the propensity to develop or aggravate, i.e. degree of, thrombosis, and well-encompassed within the definition of thrombosis, because unpatented claims are given the broadest reasonable interpretation consistent with the specification.

9. Claims 1 and 7-9 are rejected under 35 U.S.C. 102(a) as being inherently anticipated by Konetschny et al. (Development of a Highly Sensitive and Specific Enzyme-linked Immunosorbent Assay for the Detection of ADAMTS-13 in Human Plasma, Blood 102 (11) Abstract #4062 (November 16, 2003)) in light of Scheiflinger et al. (US 2004/0214346 A1).

Konetschny et al. teach that von Willebrand factor (vWF) predominantly released from endothelial cells, when stimulated, are released as high molecular weight multimeric proteins having a large portion of unusually large vWF (ULVWF) which is hemostatically very active in efficiently interacting with platelet receptors and very effective in promoting platelet adhesion to sites of vascular injury. However, prolonged presence of hyperactive ULVWF leads to platelet aggregation and thrombus formation

leading to thrombosis. Konetschny et al. teach a method of detecting occurrence of thrombosis in human plasma sample by measuring the amount of vWFcp present in the sample using highly sensitive and specific enzyme-linked immunosorbent assay (ELISA). vWF-cp (ADAMTS-13) is a metalloprotease discovered to actively regulate proteolytic degradation of ULVWF and that severe deficiency in vWFcp is also observed in acquired and hereditary TTP (1st full paragraph). In practice, Konetschny et al. teach immunologically measuring the amount of vWFcp that bound to the antibody by combining a blood sample from the patient with antibodies (anti-vWFcp) that specifically bind to vWFcp. Capture anti-vWFcp (anti-ADAMTS-13) polyclonal antibody is coated onto microtiter plate to capture vWFcp and detection anti-vWFcp MAb (242/H2) is conjugated to alkaline phosphatase so as to provide binding, detection, and measurement of vWFcp antigen present in the plasma (2nd full paragraph). Konetschny et al. show that a decrease in concentration of vWFcp manifested as a deficiency in ADAMTS-13 in a patient in comparison to healthy control subject provides indication of occurrence of thrombosis (1st and 3rd full paragraphs).

As to the recitation of "degree of thrombophilia" or "risk of thrombophilia," it is well understood that "thrombophilia" or hypercoagulability is simply a measure of the propensity to develop or aggravate, i.e. degree of, thrombosis, and well-encompassed within the definition of thrombosis, because unpatented claims are given the broadest reasonable interpretation consistent with the specification.

As to recitation of thrombosis that is manifested in "patients suffering from conditions acute or chronic myeioid leukemia, acute promyelocytic leukemia,

pulmonary, embolism, cerebral infarction, veno-occlusive disease, acute lymphocytic leukemia, and deep vein thrombosis," Scheiflinger et al. discussed supra, indeed, teach that thrombosis as taught in the method of Konetschny et al. is manifested in patients suffering from cancer-associated TM in [0034]. Accordingly, it is deemed that Konetschny et al. inherently anticipates the claimed invention.

Response to Arguments

10. Applicant's arguments with respect to claims 1 and 5-9 have been considered but are moot in view of the new grounds of rejection.

Allowable Subject Matter

11. Claims 3 and 10 would be allowable if rewritten to overcome the rejections under 35 U.S.C. 112, 2nd paragraph, set forth in this Office action and to include all of the limitations of the base claim and any intervening claims.

12. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not

mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

13. Any inquiry concerning this communication or earlier communications from the examiner should be directed to GAILENE R. GABEL whose telephone number is (571)272-0820. The examiner can normally be reached on Monday, Tuesday, Thursday, 5:30 AM to 4:00 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Mark L. Shibuya can be reached on (571) 272-0806. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/GAILENE R. GABEL/
Primary Examiner, Art Unit 1641

May 31, 2010